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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,732	12/19/2001	William M. Pardridge	0180.0029	8416

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EXAMINER	
LAMBERTSON, DAVID A	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,732	PARDRIDGE, WILLIAM M.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 23-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 23-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed December 29, 2003. Amendments were made to the claims.

Claims 1-10 and 23-29 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, mailed September 23, 2003, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 23-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This is a new rejection that is necessitated by amendment.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is

a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), and the most relevant factors are indicated below:

Nature of the invention. The nature of the invention is a receptor specific liposome expressing an "eye-specific" gene, where the liposome is used to direct the "eye-specific" gene across the Blood-Retinal Barrier (BRB) or the ocular membrane. The asserted use of the liposome is a method of using the "eye-specific" gene for diagnostic purposes. Applicant has clearly set forth in their arguments that the specification is enabled for diagnostic methods, and is not necessarily directed to methods of gene therapy. As a result, the skilled artisan must be able to use the claimed liposome for the expression of an "eye-specific" gene as a diagnostic agent.

Scope of the invention. The scope of the invention is very broad, requiring that the expression of any "eye-specific" gene be enabled for at least one specific diagnostic tool. Specifically, the claimed receptor-specific liposome must be used to target an "eye-specific" gene across the BRB or across the ocular cell membrane, where the expression of the "eye-specific" gene is diagnostic of something (e.g., a disease condition, etc.). This encompasses a broad number of genes that must have an application to the diagnosis of at least one condition.

State of the art. The State of the art is silent with regard to the use of "eye-specific" genes as diagnostic tools. There is no teaching in the art that would direct the skilled artisan as to how the expression of any "eye-specific" gene (e.g., arrestin) would be diagnostic of anything. While applicant's liposome may be useful in getting an "eye-specific" gene across the BRB or the ocular cell membrane, it is unclear what non-therapeutic (i.e., diagnostic) purpose this might

serve. As a result, the skilled artisan would not know how to use the claimed liposome for a diagnostic purpose after consulting the art, and would thus turn to the instant specification.

Number of working examples and Guidance provided by applicant. The instant specification provides no guidance as to the use of an "eye-specific" gene for diagnostic purposes. There are no examples in the specification of the targeting of an "eye-specific" gene across the BRB followed by its subsequent expression, let alone any guidance as to which genes can be used to diagnose a given particular condition. Applicant only states that "[T]he therapeutic gene which is encapsulated within the liposome can be any of the common therapeutic genes which are used to express therapeutic and diagnostic agents" (see for example paragraph [0039] as referred to in Applicant's arguments) as support for an enabling disclosure of using the "eye-specific" genes for diagnostic purposes; there is no indication of what the therapeutic genes are diagnostic of. As a result, the skilled artisan would be at a loss as to what the liposome can be used to diagnose.

Unpredictability of the art and Amount of experimentation required. Applicant asserts in their arguments that the claimed liposome can be used for diagnostic purposes. However, the claims require that the cells deliver an "eye-specific" gene, and it is unclear what any "eye-specific" gene is diagnostic of (for example, if arrestin is targeted across the BRB, what does this diagnose?). Thus, in order to use the claimed invention as a diagnostic, the skilled artisan would have to experimentally determine what each "eye-specific" gene is diagnostic of, when expressed from an exogenous source. This represents a vast amount of undue and unpredictable trial and error experimentation, basically requiring that the skilled artisan empirically determine

how to use the invention at its most rudimentary level. Because the skilled artisan cannot use the invention as claimed, the invention is not enabled.

Claims 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. **This rejection is maintained for the reasons set forth in the previous Office Action.**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 and 23-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection that is necessitated by amendment.**

Claims 1-10 and 23-29 recite the term "eye-specific gene" in the claims. It is unclear what the metes and bounds of this term are because it appears nowhere in the specification. Without a clear definition as to what makes a gene "eye-specific," it is impossible to determine what the limitations of the claims are.

Claim 5 recites the limitation "said therapeutic gene" in the claim. There is insufficient antecedent basis for this limitation in the claim.

Response to Arguments Concerning Claim Rejections - 35 USC § 112

Applicant's arguments filed December 29, 2003 have been fully considered but they are not persuasive. Applicant provides the following grounds of traversal:

1. Applicant asserts that the invention is not necessarily directed to therapeutic purposes, but can instead be used for diagnostic purposes. Specifically, Applicant states, "the invention simply involves delivery of eye-specific genes to ocular cells wherein the genes that are delivered are known by those of skill in the art to be of potential therapeutic or diagnostic value in treating eye disorders." See for example, Page 8, third full paragraph of Applicant's response.

2. Applicant further asserts that the claimed invention is not limited to a composition for use in gene therapy. Applicant specifically points to paragraphs 12 and 39 of the instant specification, where it indicates that the genes contained within the liposomes can be used for diagnostic purposes.

Applicant's arguments are not convincing for the following reasons:

1. First, it is noted that claims 23 and 24 are still directed to pharmaceutical compositions. The term "pharmaceutical" by definition relates to medicinal compositions, which are not diagnostic by nature. As such, these claims still read on gene therapy, contrary to Applicant's assertion that they do not. Second, it is noted that the specification is replete with references to the delivery of "therapeutic genes," and that the only location where the concept of diagnosis is brought up is in the two specific lines referred to by Applicant. Although the Office accepts this as an asserted utility, the instant specification does not provide an enabling disclosure for the claims. The specific points regarding this matter are addressed in the rejection under 35 USC § 112, first paragraph, set forth above. Briefly, it is set forth that the claimed invention is not enabled for

diagnostic purposes because there is no guidance in either the prior art or the instant specification as to how or what to diagnose with any given "eye-specific" gene. This lack of guidance is evident in Applicant's own statement indicating that "the genes that are delivered are...of *potential* therapeutic or diagnostic value" (emphasis added). It is clear from this statement that it is unknown which genes can be used to diagnose a particular condition. As such, Applicant's argument that the specification is enabled for diagnostic purposes is not found convincing.

2. The claimed invention may not be limited to a composition for use in gene therapy, but it still encompasses a therapeutic composition. This is especially true for claims 23 and 24, which recite that the composition is pharmaceutical (i.e., medicinal) in nature; this certainly indicates a therapeutic connotation to the composition. The issues regarding the nature of the composition as a diagnostic agent are addressed above in section (1), as well as in the rejection that has been necessitated by amendment.

In conclusion, Applicant has not provided a convincing argument that (a) claims 23 and 24 do not read on compositions for use in gene therapy and (b) that the claims are enabled for using an "eye-specific" gene as a diagnostic agent. As a result, the claims are rejected under 35 USC 112, first paragraph as lacking enablement.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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AU 1636

JAMES KETTER
PRIMARY EXAMINER